

date of Reference 1. LAC

11/17/2009

PTO/SB/08A (08-03)

Approved for use through 07/31/2006. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Sheet 1 of 1

**Complete if Known**

Application Number	
Filing Date	Sept. 16, 2003
First Named Inventor	Levon ARAKELYAN
Art Unit	
Examiner Name	
Attorney Docket Number	Q71975

**U. S. PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code <sup>2</sup> (if known)			
		US- 6,041,788 B1	03-28-2000	Liji Shen	
		US- 5,657,255 B1	08-12-1997	Fink et al	
		US- 5,808,918 B1	09-15-1998	Fink et al	
		US- 6,081,786 B1	06-27-2000	Barry et al	
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			

**FOREIGN PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T <sup>6</sup>
		Country Code <sup>3</sup> -Number <sup>4</sup> -Kind Code <sup>5</sup> (if known)				
		WO 02/051354 A2	07-04-2002	Robert Becker		
		WO 97/44752 A1	11-27-1997	Kornman et al		
		WO 01/00083 A1	01-04-2001	Thomas et al		

Examiner Signature	/Lori Clow/	Date Considered	11/17/2009
-----------------------	-------------	--------------------	------------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. <sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /LC/

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO		<b>Complete if Known</b>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (Use as many sheets as necessary)		Application Number	
		Filing Date	Sept. 16, 2003
		First Named Inventor	Levon ARAKELYAN
		Art Unit	
		Examiner Name	
Sheet 1	of 5	Attorney Docket Number	Q71975

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	1.	FDA, CENTER FOR DRUG EVALUATION AND RESEARCH (CDER), Drug Development Process for Investigational New Drugs, Revised March 6, 1998, <a href="http://www.fda.gov/cder/handbook/develop.htm">http://www.fda.gov/cder/handbook/develop.htm</a> , pp.3-28	
	2.	DEPARTMENT OF HEALTH AND HUMAN SERVICES, FDA, International Conference on Harmonization: Guidance on General Considerations for Clinical Trials, Federal Register Wednesday, December 17, 1997, pp. 66113-66119, Vol. 62, No. 242	
	3.	E.A. EISENHAUER et al, Phase-I clinical trial design in cancer drug development, J Clin Oncol, Feb., 2000, pp. 684-692, vol. 18(3)	
	4.	R. SIMON et al, Accelerated titration designs for Phase-I clinical trials in oncology, J Natl Cancer Inst, Aug. 6, 1997, pp. 1138-1147, vol. 89(15)	
	5.	J.M. COLLINS et al, Potential roles for pre-clinical pharmacology in Phase-I clinical trials, Cancer Treat Rep, Jan., 1986, pp. 73-80, vol.70(1)	
	6.	Z. AGUR et al, Effect of the dosing interval on survival and myelotoxicity in mice treated by Cytosine arabinoside, Eur. J. Cancer, 1992, pp. 1085-1090, vol. 28A(6/7)	
	7.	L. COJOCARU et al, Theoretical analysis of interval drug dosing for cell-cycle-phase-specific drugs, Math. Biosci., 1992, pp. 85-97, vol. 109	
	8.	P. UBEZIO et al, Increasing 1-b-D-Arabinofuranosylcytosine efficacy by scheduled dosing intervals based on direct measurement of bone marrow cell kinetics, Cancer Res, 1994, pp. 6446-6451, vol. 54	
	9.	Z. AGUR, Resonance and anti-resonance in the design of chemotherapeutic schedules. Jour. Theor. Medicine, 1998, pp. 237-245, vol. 1	
	10	Z. AGUR, Clinical trials of Zidovudine in HIV infection, Lancet, Dec. 9, 1989, p.1400, vol. 2(8676)	

Examiner Signature	/Lori Clow/	Date Considered	11/17/2009
--------------------	-------------	-----------------	------------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /LC/

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (Use as many sheets as necessary)		<b>Compleat if Known</b>	
		Application Number	
		Filing Date	Sept. 16, 2003
		First Named Inventor	Levon ARAKELYAN <span style="float: right;">JAN 06 2004</span>
		Art Unit	
		Examiner Name	
Sheet <b>2</b>	of <b>5</b>	Attorney Docket Number	Q71975

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	11	Z. AGUR, Use of mathematical models for analyzing host-specific parasitaemia profiles in African trypanosomes, Parasitology Today, 1992, pp. 128-129, vol. 8	
	12	R. NOREL et al, A model for the adjustment of the mitotic clock by cyclin and MPF levels. Science, 1991, pp. 1076-1078, vol. 251	
	13	Z. AGUR et al, Zidovudine toxicity to murine bone marrow may be affected by the exact frequency of drug administration, Exp. Hematol, 1991, pp. 364-368, vol. 19	
	14	Z. AGUR, Fixed points of majority rule cellular automata applied to plasticity and precision of the immune response, Complex Systems, 1991, pp. 351-356, vol. 5	
	15	Z. AGUR et al, Maturation of the humoral immune response as an optimization problem, Proc. R. Soc. Lond. B, 1991, pp. 147-150, vol. 245	
	16	L.H. HARNEVO et al, Drug resistance as a dynamic process in a model for multi-step gene amplification under various levels of selection stringency, Cancer Chemo Pharmacol, 1992, pp. 469-476, vol. 30	
	17	R. MEHR et al, Bone marrow regeneration under cytotoxic drug regimens: behaviour ranging from homeostasis to unpredictability in a model for hemopoietic differentiation, BioSystems, 1992, pp. 231-237, vol. 26/4	
	18	Z. AGUR et al, Pulse mass Measles vaccination across age cohorts, Proc. Nat. Acad. Sci. USA, 1993, pp. 11698-11702, vol. 90	
	19	Z. AGUR et al, Use of knowledge on (fn) series for predicting optimal chemotherapy treatment, Random & Computational Dynamics, 1994, pp. 279-286, vol. 2(3&4)	
	20	Z. AGUR et al, AZT effect on the Bone Marrow-a new perspective on the Concorde Trials, Jour. Biol. Sys, 1995, pp. 241-251, vol. 3(1)	

Examiner Signature	/Lori Clow/	Date Considered	11/17/2009
--------------------	-------------	-----------------	------------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /LC/

Substitute for form 1449/PTO		<b>Complete if Known</b>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (Use as many sheets as necessary)		Application Number	
		Filing Date	Sept. 16, 2003
		First Named Inventor	Levon ARAKELYAN
		Art Unit	
		Examiner Name	
Attorney Docket Number	Q71975		
Sheet 3	of 5		

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	21	R. MEHR et al, Temporal stochasticity leads to nondeterministic chaos in a model for blood cell production. in: "Fluctuations and Order: The New Synthesis", 1996, pp. 419-427, Springer, New-York	
	22	Z. AGLIR, Mathematical modeling of cancer chemotherapy: investigation of the resonance phenomenon, Adv. in Math. Pop. Dynamics-Molecules, Cells, Man, Series in Math. Biol.	
	22	(con't) pp. 571-578, vol. 6	
	23	D. HART et al, The growth law of primary breast cancer tumors as inferred from mammography screening trials, Br J Can, 1998, pp. 382-387, vol. 78(3)	
	24	E. SHOCHAT et al, Using Computer Simulations for Evaluating The Efficacy of Breast Cancer Chemotherapy Protocols, Math. Models & Methods in Applied Sciences, 1999, pp. 599-615, vol. 9(4)	
	25	K. SKOMOROVSKI et al, New TPO treatment schedules of increased safety and efficacy: pre-clinical validation of a thrombopoiesis simulation model, Br J Haematol, Nov., 2003, pp. 683-691, vol. 123(4)	
	26	L. ARAKELYAN et al, A computer algorithm describing angiogenesis and vessel maturation and its use for studying the effects of anti-angiogenic and anti-maturation therapy on vascular tumor growth, Angiogenesis, 2002, pp. 203-214, vol. 5	
	27	R. SIMON, Bayesian design and analysis of active controlled clinical trials, Biometrics, 1999, pp. 484-487, vol. 55	
	28	R. SIMON, Some practical aspects of the interim monitoring of clinical trials, Statistics in Medicine, 1994, pp. 1401-1409, vol. 13	
	29	R. SIMON, Therapeutic equivalence trials, Handbook of Statistics in Clinical Oncology, 2001, pp. 173-187, Marcel Dekker, New York	

Examiner Signature	/Lori Clow/	Date Considered	11/17/2009
--------------------	-------------	-----------------	------------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /LC/

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (Use as many sheets as necessary)		<b>Complete if Known</b>	
		Application Number	
		Filing Date	Sept. 16, 2003
		First Named Inventor	Levon ARAKELYAN
		Art Unit	
		Examiner Name	
Sheet 4	of 5	Attorney Docket Number	Q71975

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	30	A. ILIADIS et al, Optimizing Drug Regimens in Cancer Chemotherapy by an Efficacy-Toxicity Mathematical Model, Computers and Biomedical Research, 2000, pp. 211-226, vol. 33	
	31	F.L. PEREIRA et al, A new optimization based approach to experimental combination chemotherapy, Frontiers Med Biol Engng, 1995, pp. 257-268, vol. 6(4)	
	32	C. VEYRAT-FOLLET et al, Clinical trial simulation of docetaxel in patients with cancer as a tool for dosage optimization, Clin Pharmacol Ther, Dec., 2000, pp. 677-687vol. 68/6	
	33	RS ACHARYA, et al, Development of optimal drug administration strategies for cancer-chemotherapy in the framework of systems theory, Int J Biomed Comput,	
	33	(con't) March-April, 1984, pp. 139-150, vol. 15(2)	
	34	N. Stallard et al, Sequential designs for phase III clinical trials incorporating treatment selection, Stat Med, Mar., 2003, pp. 689-703, vol. 22(5)	
	35	JV GOBBURU et al, Application of modeling and simulation to integrate clinical pharmacology knowledge across a new drug application, Int J Clin Pharmacol Ther,	
	35	(con't) July, 2002, pp. 281-288, -vol. 40(7)	
	36	P. BAUER et al, Combining different phases in the development of medical treatments within a single trial, Stat Med, July, 1999, pp. 1833-1848, vol. 18(14)	
	37	E. ARDIZZONE et al, Artificial intelligence techniques for cancer treatment planning, Med Inform (Lond), Jul-Sept., 1988, pp. 199-210, vol. 13(3)	

Examiner Signature	/Lori Clow/	Date Considered	11/17/2009
--------------------	-------------	-----------------	------------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.  
 1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached.  
 This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /LC/

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO  <b>INFORMATION DISCLOSURE  STATEMENT BY APPLICANT</b>  <i>(Use as many sheets as necessary)</i>		<b>Complete if Known</b>	
		Application Number	
		Filing Date	Sept. 16, 2003
		First Named Inventor	Levon ARAKELYAN
		Art Unit	
		Examiner Name	
Sheet 5	of 5	Attorney Docket Number	Q71975

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	38	D. BERRY, Adaptive Trials and Bayesian Statistics in Drug Development, Biopharmaceutical Report, 2001, pp. 1-11 vol. 9(2)	
	39	D. BERRY, General Keynote: Clinical Trial Design, Gynecological Oncology, 2003, pp. S114-S116, vol. 88	
	40	E. TRIMBLE, Discussion: Current Issues in the Design of Ovarian Cancer Treatment Trials, Gynecological Oncology, 2003, pp. S122-S123, vol. 88	

Examiner Signature	/Lori Clow/	Date Considered	11/17/2009
--------------------	-------------	-----------------	------------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.  
1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached.  
This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /LC/